

CURRICULUM VITAE

Name

David J. FitzGerald

Current Position

Chief, Biotherapy Section Laboratory of Molecular Biology Division of Basic Science National Cancer Institue, NIH

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Education

Trinity College, Dublin, Ireland BA Mod 1977 Microbiology
U of Cincinnati, Col of Med, OH PhD 1982 Microbiology

Employment

1982 - 1984Staff Fellow, LMB, DCBDC, NCI, NIH1985 - 1987Senior Staff Fellow, LMB, DCBDC, NCI, NIH1987 - 1994Microbiologist, LMB, DCBDC, NCI, NIH1994-presentChief, Biotherapy Section, LMB, DBS, NCI, NIH

Honors

January 1980 Awarded the Albert J. Ryan Fellowship.

June 1991 NIH Director's Award

June 1992 Pierce Immunotoxin Award, at The Third International

Immunotoxin Meeting, Orlando, FL.

July 1994 Chair, Gordon Conference, Drug Carriers in Medicine &

July 1994 *Biology.*

September 1995 February 1999 NIH Award of Merit

Awarded NCI Intramural Research Award (IRA)

Teaching Experience

Was invited to teach a two-week (September - October, 1988) course on immunotoxins at the Shanghai Institute of Biochemistry (joint U.S. National Academy of Science and Chinese

Academy of Science program).

Editorial Boards

Infection and Immunity (1987-1989)

Journal of National Cancer Institute (1990-1994)

Journal of Pharmaceutical Sciences

Journal of Bioconjugate Chemistry (1990-1994)

Journal of Drug Targeting Therapeutic Immunity

Journal of Biological Chemistry (1996-

Peer Review Experience

Member of Study Section for Tropical

Medicine and Parasitology, October 1986

Member of special study section to review toxin-based grant proposals, July 1988 American Cancer Society, Ad Hoc Reviewer for

Immunotherapy Study Section, Spring 1991

Clinical Investigation

Co-investigator on FDA-approved protocol

with PE-ANTI-TAC to treat patients with adult-

T-cell leukemia,

IND #BB IND 2174

(NSC 600665).

Co-investigator on FDA-approved protocol

with OVB3-PE to treat patients with ovarian IND #IND2688 (NSC 615048).

cancer,

Co-investigator on FDA-approved protocol with LMB-1 to treat patients with adenocarcinomas IND #5017 (NSC 651311).

Co-investigator on Phase I application for IND of

immunotoxin directed to CD22+ leukemias and lymphomas (IND/NSC numbers not yet available).

Committee Experience

An original member and presently serving on NCI's

"Technology Review Group". Responsible for reviewing all new decisions about invention reports and making strategic

how to prosecute NCI's existing patent

portfolio.

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Societies

AAAS

American Society for Biochemistry and

Molecular Biology

Patents

Pastan, I., Willingham, M.C., and FitzGerald, D.J.:

Pseudomonas

exotoxin conjugate immunotoxins.

U.S.A., D.H.H.S.) (Filed January 26, 1984.) Granted U.S. (Assignee:

Patent #4,545,985, October 8, 1985.

Pastan, I., FitzGerald, D.J.P., and Willingham, M.C.:

Monoclonal antibody against ovarian cancer cells

(OVB3). Patent

Pastan.

#4,806,494, February 21, 1989.

Pastan, I., Adhya, S., and FitzGerald, D.J.P.: Recombinant

Pseudomonas exotoxin: Construction of an active immunotoxin

with low

side effects. Patent #4,892,827, January 9, 1990.

Biorn, M.J., FitzGerald, D.J., Frankel, A.E., Laird, W.J.,

I.H., Ring, D.B., Willingham, M. C., and Windelhake, J. L.:

Anti-human ovarian cancer immunotoxins and methods of use thereof.

(Assignee: Cetus Corporation) (Filed July 6, 1987.)

Granted U.S. Patent #4,958,009, September 18, 1990.

Pastan, I., FitzGerald, D., and Ogata, M.: Selectively

cytotoxic IL-4-PE40 #5,082,927, D.H.H.S.) (Filed May 12, 1989.) Granted U.S. Patent

fusion protein. (Assignee: U.S.A., January 21, 1992.

Berger, E.A., Fuerst, T.R., Pastan, I., FitzGerald, D.,

Mizukami, T., and

specific

Chaudhary, V.K.: CD-4/cytotoxic gene

fusions. Patent #5,206,353, (Assignee: U.S.A., D.H.H.S.) (Filed July 22, 1988.) Granted U.S. Patent #5,206,353, April 27, 1993.

Pastan, I.H., Trevor, P., FitzGerald, D.J., Debinski, W., and Siegall, C.:

Recombinant chimeric proteins deliverable across

ellular membranes into cytosol of target cells. (Assignee:

U.S.A., D.H.H.S.) (Filed March 4, 1991.) Granted U.S. Patent #5,328,984, July 12, 1994.

Berger, E.A., Moss, B., Fuerst, T.R., Pastan, I., FitzGerald, D.,

Mizukami, T., and Chaudhary, V.K.: Cytotoxic agent against

1993.) Granted U.S. Patent #5,428,143, June 27, 1995. virus infection. (Assignee: U.S.A.) (Filed February 25,

> Pastan, I., Chaudhary, V.K., and FitzGerald, D.: P. exotoxin fusion proteins have COOH-terminal alterations which increase cytotoxicity. (Assignee: U.S.A., D.H.H.S.) (Filed Granted U.S. Patent #5,458,878, October 17, May 14, 1990.)

1995.

Pastan, I., FitzGerald, D., and Chaudhary, V.K.: Pseudomonas exotoxins (PE) and conjugates thereof having lower animal toxicity with high cytocidal activity through substitution of positively (Filed October 1, 1993.) Granted U.S. Patent #5,512,658, charged amino acids. (Assignee: U.S.A., D.H.H.S.) 30, 1996. April

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BIBLIOGRAPHY

- 1. FitzGerald, D.J.P., Morris, R.E., and Saelinger, C.B.: Receptor-mediated internalization of *Pseudomonas* toxin by mouse fibroblasts. *Cell* 21: 867-873, 1980.
- FitzGerald, D.J.P., Morris, R.E., and Saelinger, C.B.: The essential role of calcium in cellular internalization of *Pseudomonas* toxin. *Infect. Immun.* 35: 715-720, 1982.
- FitzGerald, D.J.P., Padmanabhan, R., Pastan, I., and Willingham, M.C.: Adenovirus-induced release of epidermal growth factor and *Pseudomonas* toxin into the cytosol of KB cells during receptor-mediated endocytosis. *Cell* 32: 607-617, 1983.
- FitzGerald, D.J.P., Trowbridge, I.S., Pastan, I., and Willingham, M.C.: Enhancement of toxicity of antitransferrin receptor antibody *Pseudomonas* exotoxin conjugates by adenovirus. *Proc. Natl. Acad. Sci.* USA 80: 4134-4138, 1983.
- Willingham, M.C., Haigler, H.T., FitzGerald, D.J.P., Gallo, M.G., Rutherford, A.V., and Pastan, I.: The morphologic pathway of binding and internalization of epidermal growth factor in cultured cells. Exp. Cell Res. 146: 163-175, 1983.
- Zoon, K.C., Arnheiter, H., Zur Nedden, D., FitzGerald, D.J.P., and Willingham, M.C.: Human interferon alpha enters cells by receptor-mediated endocytosis. *Virology* 130: 195-203, 1983.
- FitzGerald, D.J.P., Morris, R.E., and Saelinger, C.B.: Inhibition of *Pseudomonas* toxin internalization by methylamine. *Rev. Infec. Dis.* 5: Suppl. S985-991, 1983.
- 8. FitzGerald, D.J.P., Waldmann, T.A., Pastan, I., and Willingham, M.C.: PE-anti-Tac: a cell-specific immunotoxin active against cells expressing the human T-cell growth factor receptor. *J. Clin. Invest.* 74: 966-971, 1984.
- 9. Seth, P., FitzGerald, D.J.P., Willingham, M.C., and Pastan, I.: Role of a low pH environment in adenovirus enhancement of the toxicity of a *Pseudomonas* exotoxin epidermal growth factor conjugate. *J. Virol.* 51: 650-655, 1984.
- Akiyama, S., Gottesman, M.M., Hanover, J.A., FitzGerald, D.J.P., Willingham, M.C., and Pastan, I.: Verapamil enhances the toxicity of an epidermal growth factor *Pseudomonas* exotoxin conjugate. *J. Cell Physiol.* 120: 271-279, 1984.
- 11. Seth, P., FitzGerald, D., Ginsberg, H., Willingham, M., and Pastan, I.: Evidence that the penton base of adenovirus is involved in potentiation of *Pseudomonas* exotoxin conjugated to epidermal growth factor. *Mol. Cell. Biol.* 4: 1528-1533, 1984.
- 12. Akiyama, S., Seth, P., Pirker, R., FitzGerald, D., Gottesman, M.M., and Pastan, I.: Potentiation of cytotoxic activity of immunotoxins on cultured human cells. *Cancer Res.* 45: 1005-1007, 1985.
- 13. Pirker, R., FitzGerald, D.J., Hamilton, T.C., Ozols, R.F., Willingham, M.C., and Pastan, I.: Anti-transferrin receptor antibody linked to *Pseudomonas* exotoxin as a model immunotoxin in human ovarian carcinoma cell lines. *Cancer Res.* 45: 751-757, 1985.
- 14. FitzGerald, D.J.P.: Transport of adenovirus and toxin conjugates into cells via the common pathway of receptor-mediated endocytosis. *Microbiology* 85-90, 1985.

- 15. Pirker, R., FitzGerald, D.J., Hamilton, T.C., Ozols, R.F., Laird, W., Frankel, A.E., Willingham, M.C., and Pastan, I.: Characterization of immunotoxins active against ovarian cancer cell lines. *J. Clin. Invest.* 76: 1261-1267, 1985.
- 16. Zoon, K.C., Arnheiter, H., Zur Nedden, D., FitzGerald, D.J., and Willingham, M.C.: Procedures for measuring receptor-mediated binding and internalization of human interferon. In *Methods of Enzymology* 119: 332-339. 1986.
- 17. Pastan, I., Seth, P., FitzGerald, D., and Willingham, M.C.: Adenovirus entry into cells: Some new observations on an old problem. In Notkins, A.L. and Oldstone, M.B.A. (Eds.): *Concepts in Viral Pathogenesis*, Vol. II. New York, Springer Verlag, 1986, pp. 141-146.
- 18. FitzGerald, D.J., Willingham, M.C., and Pastan, I.: Anti-tumor effects of an immunotoxin made with *Pseudomonas* exotoxin in a nude mouse model of human ovarian cancer. *Proc. Natl. Acad. Sci. USA* 83: 6627-6630, 1986.
- 19. Pastan, I., Willingham, M.C., and FitzGerald, D.J.P.: Immunotoxins. Cell 47: 641-648, 1986.
- 20. Seth, P., FitzGerald, D., Willingham, M.C., and Pastan, I.: Pathway of adenovirus entry into cells. In Crowell, R. and Lonberg-Holm, K. (Eds.): *Virus Attachment and Entry Into Cells*. Washington, D.C., American Society for Microbiology, 1986, pp. 191-
- 21. Hwang, J., FitzGerald, D.J.P., Adhya, S., and Pastan, I.: Functional domains of *Pseudomonas* exotoxin identified by deletion analysis of the gene expressed in *E. coli. Cell* 48: 129-136, 1987.
- 22. FitzGerald, D.J.P., Bjorn, M.J., Ferris, R.J., Winkelhake, J.L., Frankel, A.E., Hamilton, T.C., Ozols, R.F., Willingham, M.C., and Pastan, I.: Antitumor activity of an immunotoxin in a nude mouse model of human ovarian cancer. *Cancer Res.* 47: 1407-1410, 1987.
- 23. Willingham, M.C., FitzGerald, D.J., and Pastan, I.: *Pseudomonas* exotoxin coupled to a monoclonal antibody against ovarian cancer inhibits the growth of human ovarian cancer cells in a mouse model. *Proc. Natl. Acad. Sci. USA* 84: 2474-2478, 1987.
- 24. FitzGerald, D.J., Willingham, M.C., Cardarelli, C.O., Hamada, H., Tsuruo, T., Gottesman, M.M., and Pastan, I.: A monoclonal antibody *Pseudomonas* toxin conjugate that specifically kills multidrug-resistant cells. *Proc. Natl. Acad. Sci. USA* 84: 4288-4292, 1987.
- 25. Lyall, R.M., Hwang, J., Cardarelli, C., FitzGerald, D., Akiyama, S.-I., Gottesman, M.M., and Pastan, I.: Isolation of human KB cell lines resistant to epidermal growth factor *Pseudomonas* exotoxin conjugates. *Cancer Res.* 47: 2961-2966, 1987.
- 26. Chaudhary, V.K., FitzGerald, D.J., Adhya, S., and Pastan, I.: Activity of a recombinant fusion protein between transforming growth factor type α and *Pseudomonas* toxin. *Proc. Natl. Acad. Sci. USA* 84: 4538-4542, 1987.
- 27. Cryz, S.J., Jr., Furer, E., Sadoff, J.C., Germanier, R., Pastan, I., Willingham, M.C., and FitzGerald, D.J.P.: The use of *Pseudomonas aeruginosa* toxin A in the construction of conjugate vaccines and immunotoxins. *Rev. Infect. Dis.* 9: S644-749, 1987.
- 28. Pirker, R., FitzGerald, D., Willingham, M.C., and Pastan, I.: Immunotoxins and endocytosis. *Lymphokines* 14: 361-382, 1987.
- 29. FitzGerald, D.J.P.: Construction of immunotoxins using *Pseudomonas* exotoxin A. *Methods Enzymol.* 151: 139-145, 1987.

- 30. Griffin, T.W., Childs, L.R., FitzGerald, D.J., and Levin, L.V.: Enhancement of the cytotoxic effect of anti-carcinoembryonic antigen immunotoxins by adenovirus and carboxylic ionophones. *J. Natl. Cancer Inst.* 79: 679-685, 1987.
- 31. Lorberboum-Galski, H., FitzGerald, D.J.P., Chaudhary, V.K., Adhya, S., and Pastan, I.: Cytotoxic activity of an interleukin 2-Pseudomonas exotoxin chimeric protein produced in E. coli. Proc. Natl. Acad. Sci. USA 85: 1922-1926, 1988.
- 32. Kondo, T., FitzGerald, D., Chaudhary, V.K., Adhya, S., and Pastan, I.: Activity of immunotoxins constructed with modified *Pseudomonas* exotoxin A lacking the cell recognition domain. *J. Biol. Chem.* 263: 9470-9475, 1988.
- 33. Chaudhary, V.K., Xu, Y.H., FitzGerald, D., Adhya, S., and Pastan. I.: Role of domain II of *Pseudomonas* exotoxin in the secretion of proteins into the periplasm and medium by *Escherichia coli. Proc. Natl. Acad. Sci. USA* 85: 2939-2943, 1988.
- 34. FitzGerald, D., Willingham, M.C., and Pastan, I.: *Pseudomonas* exotoxinimmunotoxins. In Frankel, A. (Ed.): *Immunotoxins*. Martin Nijoff B.V., 1988, pp. 161-
- 35. Pirker, R., FitzGerald, D.J., Willingham, M.C., and Pastan, I.: Enhancement of the activity of immunotoxins made with either ricin A chain or *Pseudomonas* exotoxin in human ovarian and epidermoid carcinoma cell lines. *Cancer Res.* 48: 3919-3923, 1988.
- 36. Jinno, Y., Chaudhary, V.K., Kondo, T., Adhya, S., FitzGerald, D.J., and Pastan, I.: Mutational analysis of domain I of *Pseudomonas* exotoxin. Mutations in domain I of *Pseudomonas* exotoxin which reduce cell binding and animal toxicity. *J. Biol. Chem.* 263: 13203-13207, 1988.
- 37. Chaudhary, V.K., Mizukami, T., Fuerst, T.R., FitzGerald, D.J., Moss, B., Pastan, I., and Berger, E.A.: Selective killing of HIV-infected cells by recombinant human CD4-Pseudomonas exotoxin hybrid protein.

 Nature 335: 369-372, 1988.
- 38. Gallo, M.G., Chaudhary, V.K., FitzGerald, D.J., Willingham, M.C., and Pastan, I.: Cloning and . expression of the H chain V region of antibody OVB3 that reacts with human ovarian cancer. *J. Immunol.* 141: 1034-1040, 1988.
- 39. Bailon, P., Weber, D.V., Gately, M., Smart, J.E., Lorberboum-Galski, H., FitzGerald, D., and Pastan, I.: Purification and partial characterization of an interleukin 2- *Pseudomonas* exotoxin fusion protein. *Biotechnology* 6: 1326-1329, 1988.
- 40. Lorberboum-Galski, H., Kozak, R.W., Waldmann, T.A., Bailon, P., FitzGerald, D.J., and Pastan, I.: Interleukin 2 (IL2) PE40 is cytotoxic to cells displaying either the p55 or p70 subunit of the IL2 receptor. *J. Biol. Chem.* 263: 18650-18656, 1988.
- 41. Ogata, M., Lorberboum-Galski, H., FitzGerald, D., and Pastan, I.: IL-2-PE40 is cytotoxic for activated T lymphocytes expressing IL-2 receptors. *J. Immunol.* 141: 4224-4228, 1988.
- 42. Siegall, C.B., Chaudhary, V.K., FitzGerald, D.J., and Pastan, I.: Cytotoxic activity of an interleukin 6-Pseudomonas exotoxin fusion protein on human myeloma cells. *Proc.* Natl. Acad. Sci. USA 85: 9738-9742, 1988.
- 43. Lorberboum-Galski, H., Barrett, L.V., Kirkman, R.L., Ogata, M., Willingham, M.C., FitzGerald, D.J., and Pastan, I.: Cardiac allograft survival in mice treated with IL-2- PE40. *Proc. Natl. Acad. Sci. USA* 86: 1008-1012, 1989.

- 44. FitzGerald, D. and Pastan, I.: Toxin conjugates: Interaction with mammalian cells. In Saelinger, C.B. (Ed.): *Trafficking of Bacterial Toxins*. CRC Press, 1989, pp. 149-163.
- 45. Case, J.P., Lorberboum-Galski, H., Lafyatis, R., FitzGerald, D., Wilder, R.L., and Pastan, I.: Chimeric cytotoxin IL2-PE40 prevents adjuvant arthritis in rats. *Proc. Natl. Acad. Sci. USA* 86: 287-291, 1989.
- 46. Pearson, J.W., FitzGerald, D.J.P., Willingham, M.C., Wiltrout, R.H., Pastan, I., and Longo, D.: Chemo-immunotoxin therapy against a human colon tumor(HT-29) xenografted into nude mice. *Cancer Res.* 49: 3562-3567, 1989.
- 47. Chaudhary, V.K., Queen, C., Junghans, R.P., Waldmann, T.A., FitzGerald, D.J., and Pastan, I.: A recombinant immunotoxin consisting of two antibody variable domains fused to *Pseudomonas* exotoxin. *Nature* 339: 394-397, 1989.
- 48. Ogata, M., Chaudhary, V.K., FitzGerald, D.J., and Pastan, I.: Cytotoxic activity of a recombinant fusion protein between interleukin 4 and *Pseudomonas* exotoxin. *Proc. Natl. Acad. Sci. USA* 86: 4215-4219, 1989.
- 49. Siegall, C.B., Chaudhary, V.K., FitzGerald, D.J., and Pastan, I.: Functional analysis of domains II, Ib, and III of *Pseudomonas* exotoxin. *J. Biol. Chem.* 264: 14256- 14261, 1989.
- 50. Pastan, I. and FitzGerald, D.: *Pseudomonas* exotoxin: chimeric toxins. *J. Biol. Chem.* 264: 15157-15160, 1989.
- 51. FitzGerald, D. and Pastan, I.: Targeted toxin-therapy for the treatment of cancer. *J. Natl. Cancer Inst.* 81: 1455-1463, 1989.
- 52. Pirker, R., FitzGerald, D.J., Raschack, M., Frank, Z., Willingham, M.C., and Pastan, I.: Enhancement of the activity of immunotoxins by analogues of verapamil. *Cancer Res.* 49: 4791-4795, 1989.
- 53. Berger, E.A., Clouse, K.A., Chaudhary, V.K., Chakrabarti, S., FitzGerald, D.J., Pastan, I., and Moss, B.: CD4-Pseudomonas exotoxin hybrid protein blocks the spread of human immunodeficiency virus infection in vitro and is active against cells expressing the envelope glycoproteins from diverse primate immunodeficiency retroviruses. *Proc. Natl. Acad. Sci. USA* 86: 9539-9543, 1989.
- Roberge, F.G., Lorberboum-Galski, H., Le Hoang, P., de Smet, M., Chan, C.C., FitzGerald, D., and Pastan,
 I.: Selective immunosuppression of activated T cells with the chimeric toxin IL-2-PE40. Inhibition of experimental autoimmune uveoretinitis. *J. Immunol.* 143: 3498-3502, 1989.
- 55. Jinno, Y., Ogata, M., Chaudhary, V.K., Willingham, M.C., Adhya, S., FitzGerald, D., and Pastan, I.: Domain II mutants of *Pseudomonas* exotoxin deficient in translocation. *J. Biol. Chem.* 264: 15953-15959, 1989.
- 56. Batra, J.K., Jinno, Y., Chaudhary, V.K., Kondo, T., Willingham, M.C., FitzGerald, D.J., and Pastan. I.: Antitumor activity in mice of an immunotoxin made with antitransferrin receptor and a recombinant form of *Pseudomonas* exotoxin. *Proc. Natl. Acad, Sci. USA* 86: 8545-8549, 1989.
- 57. Moss, B., Mizukami, T., Fuerst, T., Berger, E., Chaudhary, V., FitzGerald, D., and Pastan, I.: Localization of the HIV-binding region of CD4 and selective killing of HIV- infected cells with a hybrid CD4
 Pseudomonas exotoxin. In: Girard, M. and Valette, L. (Eds.). Colloque des Cent Gardes: Retroviruses of Human AIDS and Related Animal Diseases. France, Pasteur Vaccins, Marnes-La-Coquette, 1989, pp. 60-65.
- 58. Berger, E.A., Chaudhary, V.K., Clouse, K.A., FitzGerald, D.J., Pastan, I., and Moss, B.: Recombinant CD4-pseudomonas exotoxin hybrid protein: Specific cytotoxic activity against T-cell lines infected with human

- immunodeficiency virus. In Groopman, J.E., Chen, I., Essex, M., and Weiss, R. (Eds.): *Human Retroviruses, UCLA Symposia on Molecular and Cellular Biology, New Series*, Vol 119. New York, Alan R. Liss, Inc., 1989, pp. 261-270.
- 59. Chaudhary, V.K., Jinno, Y., FitzGerald, D., and Pastan, I.: *Pseudomonas* exotoxin contains a specific sequence at the carboxyl terminus that is required for cytotoxicity and resembles the endoplasmic reticulum retention sequence. *Proc. Natl. Acad. Sci. USA* 87: 308-312, 1990.
- Tomasselli, A.G., Hui, J.O., Sawyer, T.K., Staples, D.J., FitzGerald, D.J., Chaudhary, V.K., Pastan, I., and Heinrikson, R.L.: Interdomain hydrolysis of a truncated *pseudomonas* exotoxin by the human immunodeficiency virus-1 protease. *J. Biol. Chem.* 265: 408-413, 1990.
- 61. Chaudhary, V.K., Batra, J.K., Gallo, M., Willingham, M.C., FitzGerald, D.J., and Pastan, I.: A rapid method of cloning functional variable region antibody genes in *E. coli* as single chain immunotoxin. *Proc. Natl. Acad. Sci. USA* 87: 1066-1070, 1990.
- 62. Idziorek, T., FitzGerald, D., and Pastan, I.: Low pH-induced changes in *Pseudomonas* exotoxin and its domains: Increased binding of triton X-114. *Infect. Immun.* 58: 1415- 1420, 1990.
- 63. Siegall, C.B., Nordan, R.P., FitzGerald, D.J., and Pastan, I.: Cell-specific toxicity of a chimeric protein composed of interleukin-6 and *Pseudomonas* exotoxin (IL6-PE40) on tumor cells. *Mol. Cell. Biol.* 10: 2443-2447, 1990.
- Berger, E.A., Chaudhary, V.K., Clouse, K.A., Taraquemada, D., Nicholas, J.A., Rubino, K.L., FitzGerald, D.J., Pastan, I., and Moss, B.: Recombinant CD4-*Pseudomonas* exotoxin hybrid protein displays HIV-specific cytotoxicity without affecting MHL class II-dependent functions. *AIDS Res. Hum. Retroviruses* 6: 795-804, 1990.
- 65. Kozak, R.W., FitzGerald, D.J., Atcher, R.W., Goldman, C.K., Nelson, D.L., Gansow, O.A., Pastan, I., and Waldmann, T.A.: Selective elimination *in vitro* of alloresponsive T cells to human transplantation antigens by toxin or radionucleotide conjugated anti-II- 2 receptor (Tac) monoclonal antibody. *J. Immunol.* 144: 3417-3423, 1990.
- 66. Siegall, C.B., Chaudhary, V.K., FitzGerald, D.J., and Pastan, I.: Tumor-specific cytotoxicity of the chimeric toxin TGFa-PE40 and IL6-PE40. In Dinarelli, C.A., Kluger, M., Oppenheim, J., and Powanda, M. (Eds.): *Physiological and Pathological Effects of Cytokines*. New York, Alan R. Liss, Inc., 1990, pp. 401-406.
- 67. Tomasselli, A.G., Hui, J.O., Sawyer, T.K., Staples, D.J., Bannow, C.A., Chaudhary, V.K., Fryling, C.M., Pastan, I., FitzGerald, D.J., and Heinrikson, R.L.: Proteases from HIV and AMV show distinct specificities in the hydrolysis of multidomain protein substrates. *J. Virol.* 64: 3157-3161, 1990.
- 68. FitzGerald, D., Idziorek, T., Batra, J.K., Willingham, M.C., and Pastan, I.: Antitumor activity of thioether linked immunotoxin: OVB3-PE. *Bioconjug. Chem.* 1: 264-268, 1990.
- 69. Chaudhary, V.K., Jinno, Y., Gallo, M.G., FitzGerald, D., and Pastan, I.: Mutagenesis of *Pseudomonas* exotoxin in identification of sequences responsible for animal toxicity. *J. Biol. Chem.* 265: 16306-16310, 1990.
- 70. Batra, J.K., Chaudhary, V.K., FitzGerald, D., and Pastan, I.: TGFα-anti-Tac(Fv)- PE40: A bifunctional toxin cytotoxic for cells with EGF or IL2 receptors. *Biochem. Biophys. Res. Commun.* 171: 1-6, 1990.
- 71. Lorberboum-Galski, H., Garsia, R.J., Gately, M., Brown, P.S., Clark, R.E., Waldmann, T.A., Chaudhary, V.K., FitzGerald, D.J.P., and Pastan, I.: IL2-PE66**cis*, a new chimeric protein cytotoxic to human activated T lymphocytes. *J. Biol. Chem.* 265: 16311-16317, 1990.

- 72. Siegall, C.B., FitzGerald, D.J., and Pastan, I.: Cytotoxicity of IL6-PE40 and derivatives on tumor cells expressing a range of IL6 receptor levels. *J. Biol. Chem.* 265: 16318-16323, 1990.
- 73. Ogata, M., Chaudhary, V.K., Pastan, I., and FitzGerald, D.J.: Processing of *Pseudomonas* exotoxin by a cellular protease results in the generation of a 37,000 Da toxin fragment that is translocated to the cytosol. *J. Biol. Chem.* 265: 20678-20685,
- 74. Batra, J.K., FitzGerald, D., Gately, M., Chaudhary, V.K., and Pastan, I.: Anti- Tac(Fv)-PE40: A single chain antibody *pseudomonas* fusion protein directed at interleukin 2 receptor bearing cells. *J. Biol. Chem.* 265: 15195-15202, 1990.
- 75. Ashorn, P., Moss, B., Weinstein, J.N., Chaudhary, V.K., FitzGerald, D.J., Pastan, I., and Berger, E.A.: Elimination of infectious HIV from human T-cell cultures by synergistic action of CD4-pseudomonas exotoxin and reverse transcriptase inhibitors.

Proc. Natl. Acad. Sci. USA 87: 8889-8893,1990.

- Siegall, C.B., FitzGerald, D.J., and Pastan, I.: Selective killing of tumor cells using EGF or TGFα-Pseudomonas exotoxin chimeric molecules. Sem. Cancer Biol. 1: 345-350, 1990.
- Kozak, R.W., Lorberboum-Galski, H., Jones, L., Puri, R.K., Willingham, M.C., Malek, T., FitzGerald, D.J., Waldmann, T., and Pastan, I.: IL2-PE40 prevents the development of tumors in mice injected with IL-2 receptor expressing EL4 transfectant tumor cells. *J. Immunol.* 145: 2766-2771, 1990.
- 78. Pai, L.H., FitzGerald, D.J., Tepper, M., Schacter, B., Spitalny, G., and Pastan, I.: Inhibition of antibody response to *Pseudomonas* exotoxin (PE) and an immunotoxin containing *Pseudomonas* exotoxin by 15-deoxyspergualin in mice. *Cancer Res.* 50: 7750-7753, 1990.
- Siegall, C.B., Schwab, G., Nordan, R.P., FitzGerald, D.J., and Pastan, I.: Expression of the interleukin 6 receptor and interleukin 6 in prostate carcinoma cells. Cancer Res. 50: 7786-7788, 1990.
- 80. Chaudhary, V.K., Gallo, M.G., FitzGerald, D.J., and Pastan, I.: A recombinant single-chain immunotoxin composed of anti-Tac variable regions and a truncated diphtheria toxin. *Proc. Natl. Acad. Sci. USA* 87: 9491-9494, 1990.
- Kreitman, R.J., Chaudhary, V.K., Waldmann, T., Willingham, M.C., FitzGerald, D.J., and Pastan, I.: The recombinant immunotoxin anti-Tac(Fv)-PE40 is cytotoxic toward peripheral blood malignant cells from patients with adult T-cell leukemia. *Proc. Natl. Acad. Sci. USA* 87: 8291-8295, 1990.
- 82. Siegall, C.B., FitzGerald, D.J., and Pastan, I.: Selective killing of IL6 receptor bearing myeloma cells using recombinant IL6-*Pseudomonas* toxin. In Potter, M. and Melchers, F. (Eds.): *Mechanisms of B-cell Neoplasia*. New York, Springer-Verlag, 1990, pp. 63-69.
- Siegall, C.B., FitzGerald, D.J., and Pastan, I.: Selective killing of IL6 receptor bearing myeloma cells using recombinant IL6-Pseudomonas toxin. Curr.Top. Microbiol. Immunol. 166: 63-69, 1990.
- 84. Heimbrook, D.C., Stirdivant, S.M., Ahern, J.D., Blaishin, N.L., Patrick, D.R., Edwards, G.M., Defeo-Jones, D., FitzGerald, D.J., Pastan, I., and Oliff, A.: Transforming growth factor-alpha Pseudomonas exotoxin fusion protein prolongs survival of nude mice bearing tumor xenografts. Proc. Natl. Acad. Sci. USA 88: 4697-4701, 1990.
- Ogata, M., Pastan, I., and FitzGerald, D.: Analysis of *Pseudomonas* exotoxin activation and conformational changes by using monoclonal antibodies as probes. *Infect. Immu*n. 59: 407-414, 1991.

- 86. Prior, T.I., Helman, L.J., FitzGerald, D.J., and Pastan, I.: Cytotoxic activity of a recombinant fusion protein between insulin-like growth factor I and *Pseudomonas* exotoxin. *Cancer Res.* 51: 174-180, 1991.
- 87. Prior, T.I., FitzGerald, D.J., and Pastan, I.: Barnase toxin A new chimeric toxin composed of *Pseudomonas* exotoxin-A and barnase. *Cell* 64: 1017-1023, 1991.
- 88. FitzGerald, D.J.: How can we target cytotoxins to destroy subclasses of nociceptors. In: Basbaum, A.I. and Besson J.-M. (Eds.): *Towards a New Pharmacoltherapy of Pain. Dahlem Konferenzen.* Chicester, England, John Wiley & Sons Ltd., 1991, pp. 69-82.
- Debinski, W., Siegall, C.B., FitzGerald, D., and Pastan, I.: Substitution of foreign protein sequences into a chimeric toxin composed of transforming growth factor alpha and pseudomonas exotoxin. Mol. Cell. Biol. 3: 1751-1753, 1991.
- Rose, J.W., Lorberboum-Galski, H., FitzGerald, D., McCarron, R., Hill, K.E., Townsend, J.J., and Pastan, I.: Chimeric cytotoxin IL2-PE40 inhibits relapsing experimental allergic encephalomyelitis. *J. Neuroimmunol.* 32: 209-217, 1991.
- 91. FitzGerald, D. and Pastan, I.: *Pseudomonas* exotoxin and derived conjugates: Interactions with mammalian cells. In Steer, C.J., and Hanover, J. (Eds.): *Intracellular Trafficking of Proteins*. England, Cambridge University Press, 1991, pp. 226-247.
- 92. Chaudhary, V.K., Moss, B., Berger, E.A., FitzGerald, D.J., and Pastan, I.: CD4-PE40: A chimeric toxin active against HIV-infected cells. In Gallo, R.C. and Jay, G. (Eds.): *The Human Retroviruses*. Orlando, FL, Academic Press, 1991, pp. 379-387.
- 93. Batra, J.K., FitzGerald, D.J., Chaudhary, V.K., and Pastan, I.: Single chain immunotoxins directed at the human transferrin receptor containing pseudomonas exotoxin A or diphtheria toxin: Anti-TFR(Fv)-PE40 and DT388-Anti-TFR(Fv). *Mol. Cell. Biol.* 11: 2200-2205, 1991.
- 94. Pai, L.H., Batra, J.K., FitzGerald, D.J., Willingham, M.C., and Pastan, I.: Anti-tumor activities of immunotoxins made of monoclonal antibody B3 and different forms of *Pseudomonas* exotoxin. *Proc. Natl. Acad. Sci. USA* 88: 3358-3362, 1991.
- 95. Siegall, C.B., Kreitman, R.J., FitzGerald, D.J., and Pastan, I.: Anti-tumor effects of IL6-*Pseudomonas* exotoxin chimeric molecules against the human hepatocellular carcinoma, PLC/PRF/5 in mice. *Cancer Res.* 51: 2831-2836, 1991.
- Heimbrook, D.C., Stirdivant, S.M., Ahern, J.D., Balishan, N.L., Patrick, D.R., Edwards, G.M., Defeo-Jones,
 D., FitzGerald, D.J., Pastan, I., and Oliff, A.: Biological activity of a transforming growth factor-alpha-Pseudomonas exotoxin fusion protein in vitro and in vivo. J. Industrial Microbiol. 7: 203-208, 1991.
- 97. Epstein, S.E., Siegall, C.B., Biro, S., Fu, Y.-M., FitzGerald, D., and Pastan, I.: Cytotoxic effects of a recombinant chimeric toxin on rapidly proliferating vascular smooth muscle cells. *Circ. Res.* 84: 778-787, 1991.
- 98. Siegall, C.B., Ogata, M., Pastan, I., and FitzGerald, D.J.: Analysis of sequences in domain II of *Pseudomonas* exotoxin A which mediate translocation. *Biochemistry* 30: 7154-7159, 1991.
- Pai, H., Gallo, M.G., FitzGerald, D.J., and Pastan, I.: Anti-tumor activity of a transforming growth factor alpha-Pseudomonas exotoxin fusion protein (TGFα-PE40). Cancer Res. 51: 2808-2812, 1991.

Puri, R.K., Ogata, M., Leland, P., Feldman, G.M., FitzGerald, D., and Pastan, I.: Expression of high affinity IL-4 receptors on murine sarcoma cells and receptor mediated cytotoxicity of tumor cells to chimeric protein between IL-4 and *pseudomonas* exotoxin. *Cancer Res.* 51: 3011-3017, 1991.

- 101. Lorberboum-Galski, H., Lafyatis, R., Case, J.P., FitzGerald, D., Wilder, R.L., and Pastan, I.: Administration of IL2-PE40 via osmotic pumps prevents adjuvant induced arthritis in rats. Improved therapeutic index of IL2-PE40 administered by continuous infusion. *Int. J. Immunopharmacol.* 13: 305-315, 1991.
- Herbort, C.P., de Smet, M.D., Roberge, F.G., Nussenblatt, R.B., FitzGerald, D., Lorberboum-Galski, H., and Pastan, I.: Treatment of corneal allograft rejection with the cytotoxin IL2-PE40. *Transplantation* 52: 470-474, 1991.
- Beraud, E., Lorberboum-Galski, H., Chan, C.C., FitzGerald, D., Pastan, I., and Nussenblatt, R.B.: Immunospecific suppression of encephalitogenic activated T lymphocytes by chimeric cytotoxin IL-2-PE40. Cell. Immunol. 133: 379-389, 1991.
- 104. Seetharam, S., Chaudhary, V., FitzGerald, D., and Pastan, I: Increased cytotoxic activity of *Pseudomonas* exotoxin and two chimeric toxins ending in KDEL. *Biol. Chem.* 266: 17376-17381, 1991.
- FitzGerald, D. and Pastan, I.: Redirecting Pseudomonas exotoxin. Sem. Cell Biol. (Redirecting Nature's Toxins) 2: 31-37, 1991.
- Brinkmann, U., Pai, L.H., FitzGerald, D.J., Willingham, M.C., and Pastan, I.: B3(Fv)-PE38KDEL, a single-chain immunotoxin that causes complete regression of a human carcinoma in mice. *Proc. Natl. Acad. Sci. USA* 88: 8616-8620, 1991.
- 107. Siegall, C.B., Epstein S., Speir, E., Hla, T., Forough, R., Maciag, T., FitzGerald, D., and Pastan, I.: Cytotoxic activity of chimeric proteins composed of acidic fibroblast growth factor and *Pseudomonas* exotoxin on a variety of cell types. FASEB J. 5: 2843-2849, 1991.
- 108. Pastan, I. and FitzGerald, D.J.: Recombinant toxins for cancer treatment. Science 254: 1173-1177, 1991.
- 109. Pai, L.H., Bookman, M.A., Ozols, R.J., Young, R.C., Smith, J.W. II, Longo, D.L., Gould, B., Frankel, A., McClay, E.F., Howell, S., Reed, E., Willingham, M.C., FitzGerald, D.J., and Pastan, I.: Clinical evaluation of intraperitoneal *pseudomonas* exotoxin immunoconjugate OVB3-PE in patients with ovarian cancer. *J. Clin. Oncol.* 9: 2095-2103, 1991.
- Chaudhary, V.K., FitzGerald, D.J., and Pastan, I.: A proper amino terminus of Diphtheria toxin is required for cytotoxicity. *Biochem. Biophys. Res. Commun.* 180: 545-551, 1991.
- Fryling, C., Ogata, M., and FitzGerald, D.: Characterization of a cellular protease that cleaves *Pseudomonas* exotoxin. *Infect. Immun.* 60: 497-502, 1992.
- Fattom, A., Shiloach, J., Bryla, D., FitzGerald, D., Pastan, I., Karakawa, W.W., Robbins, J.B., and Schneerson, R.: Comparative immunogenicity of conjugates composed of the Staphylococcus aureus type 8 capsular polysaccharide bound to carrier proteins by adipic acid dihydrazide or N-Succinimidyl-3-(2-Pyridyldithio)propionate. Infect. Immun. 60: 584-589, 1992.
- 113. Kreitman, R.J., Chaudhary, V.K., Siegall, C.B., FitzGerald, D.J., and Pastan, I.: Rational design of a chimeric toxin: An intramolecular location for the insertion of transforming growth factor α within *Pseudomonas* exotoxin as a targeting ligand. *Bioconjug. Chem.* 3: 58-62, 1992.
- Kreitman, R.J., Siegall, C.B., Chaudhary, V.K., FitzGerald, D.J., and Pastan, I.: Properties of chimeric toxins with two recognition domains: Interleukin 6 and transforming growth factor α at different locations in Pseudomonas exotoxin. Bioconjug. Chem. 3: 63-68, 1992.

- Kreitman, R.J., Siegall, C.B., FitzGerald, D.J., Epstein, J., Barlogie, B., and Pastan, I.: Interleukin 6 fused to a mutant from of *Pseudomonas* exotoxin kills malignant cells from patients with multiple myeloma. *Blood* 79: 1775-1780, 1992.
- 116. Prior, T.I., FitzGerald, D.J., and Pastan, I.: Translocation mediated by domain II of *Pseudomonas* exotoxin A: Transport of barnase into the cytosol. *Biochemistry* 31: 3555-3559, 1992.
- 117. Pastan, I., Chaudhary, V.K., and FitzGerald, D.J.: Recombinant toxins as novel therapeutic agents. *Annu. Rev. Biochem.* 61: 331-354, 1992.
- 118. Kreitman, R.J., FitzGerald, D., and Pastan, I.: Targeting growth factor receptors with fusion toxins. *Int. J. Immunopharmacol.* 14: 465-472, 1992.
- 119. FitzGerald, D., Chaudhary, V.K., Kreitman, R.J., Siegall, C.B., and Pastan, I.: Generation of chimeric toxins. In Frankel, A.E. (Ed.): Genetically Engineered Toxins. New York, Marcel Dekker, Inc., 1992, pp. 447-462.
- Pai., L.H., Batra, J.K., FitzGerald, D.J., Willingham, M.C., and Pastan, I.: Antitumor effect of B3-PE and B3-LysPE40 in a nude mouse model of human breast cancer and the evaluation of B3-PE toxicity in monkeys. Cancer Res. 52: 3189-3193, 1992.
- 121. Kounnas, M.Z., Morris, R.E., Thompson, M.R., FitzGerald, D.J., Strickland, D.K., and Saelinger, C.B.: The α₂-macroglobulin receptor/low density lipoprotein receptor-related protein binds and internalizes Pseudomonas exotoxin A. J. Biol. Chem. 267: 12420-12423, 1992.
- 122. Kreitman, R.J., Schneider, W.P., Queen, C., Tsudo, M., FitzGerald, D.J.P., Waldmann, T.A., and Pastan, I.: M1k-β(Fv)-PE40, a recombinant immunotoxin cytotoxic toward cells bearing the beta chain of the IL-2 receptor. *J. Immunol.* 149: 2810-2815, 1992.
- 123. Theuer, C.P., FitzGerald, D., and Pastan, I.: A recombinant form of *Pseudomonas* exotoxin directed at the epidermal growth factor receptor that is cytotoxic without requiring proteolytic processing. *J. Biol. Chem.* 267: 16872-16877, 1992.
- Debinski, W., Karlsson, B., Lindholm, L., Siegall, C.B., Willingham, M.C., FitzGerald, D., and Pastan, I.: Monoclonal antibody C242 *Pseudomonas* exotoxin A: A specific and potent immunotoxin with antitumor activity on a human colon cancer xenograft in nude mice. *J. Clin. Invest.* 90: 405-411, 1992.
- 125. Kasturi, S., Kihara, A., FitzGerald, D., and Pastan, I.: Alanine scanning mutagenesis identifies surface amino acids on domain II of *Pseudomonas* exotoxin required for cytotoxicity, proper folding and secretion into periplasm. *J. Biol. Chem.* 267: 23427-23433, 1992.
- Ogata, M., Fryling, C.M., Pastan, I., and FitzGerald, D.J.: Cell-mediated cleavage of *Pseudomonas* exotoxin between Arg279 and Gly280 generates the enzymatically active fragment which translocates to the cytosol. *J. Biol. Chem.* 267: 25396-25401, 1992.
- 127. FitzGerald, D.J. and Pastan, I.: *Pseudomonas* exotoxin recombinant conjugates as therapeutic agents. *Biochem. Soc. Trans.* 20: 731-734, 1992.
- 128. Puri, R. K., FitzGerald, D., Leland, P., Kozak, R. W., and Pastan, I.: In vitro and in vivo suppression of interleukin-2-activated killer cell activity by chimeric protein between interleukin-2 and Pseudomonas exotoxin. Cell. Immunol. 143: 324-334, 1992.
- 129. Brinkmann, U., Pai, L.H., FitzGerald, D.J., and Pastan, I.: Alteration of a protease-sensitive region of Pseudomonas exotoxin prolongs its survival in the circulation of mice.

- Proc. Natl. Acad. Sci. USA 89: 3065-3069, 1992.
- 130. Kreitman, R.J., Chaudhary, V.K., Kozak, R.W., FitzGerald, D.J.P., Waldmann, T.A., and Pastan, I.:

 Recombinant toxins containing the variable domains of the anti-Tac monoclonal antibody to the IL2-receptor kill malignant cells from patients with chronic lymphocytic leukemia. *Blood* 80: 2344-2352, 1992.
- Debinski, W., Jinno, Y., Siegall, C.B., FitzGerald, D.J., and Pastan, I.: Genetic manipulations in a primary structure of PE40 that enable its selective chemical derivatization. In Epenetos, A.A. (Ed.): *Monoclonal Antibodies: Applications in Clinical Oncology*. Cambridge, England, Chapman & Hall, 1993, pp. 503-511.
- Fattom, A., Schneerson, R., Watson, D.C., Karakawa, W.W., FitzGerald, D., Pastan, I., Li, X.R., Shiloach, J., Bryla, D.A., and Robbins, J.B.: Laboratory and clinical-evaluation of conjugate vaccines composed of staphylococcus-aureus type-5 and type-8 capsular polysaccharides bound to Pseudomonas-aeruginosa recombinant exoprotein-A. *Infect. Immun.* 6: 1023-1032, 1993.
- Theuer, C.P., FitzGerald, D.J., and Pastan, I.: Immunotoxins made with a recombinant form of Pseudomonas exotoxin A that do not require proteolysis for activity. Cancer Res. 53: 340-347, 1993.
- 134. Kreitman, R.J., Batra, J.K., Seetharam, S., Chaudhary, V.K., FitzGerald, D.J., and Pastan, I.: Single-chain immunotoxin fusions between anti-Tac and *Pseudomonas* exotoxin Relative importance of the two toxin disulfide bonds. *Bioconjug. Chem.* 4: 112-120, 1993.
- 135. Kreitman, R.J., Hansen, H.J., Jones, A.L., FitzGerald, D.J., Goldenberg, D.M., and Pastan, I.: Pseudomonas exotoxin-based immunotoxins containing the antibody LL2 or LL2-Fab' induce regression of subcutaneous human B cell lymphoma in mice. *Cancer Res.* 53: 819-825, 1993.
- 136. Kreitman, R.J., Chaudhary, V.K., Waldmann, T.A., Hanchard, B., Cranston, B., FitzGerald, D.J.P., and Pastan, I.: Cytotoxic activities of recombinant toxins composed of *Pseudomonas* toxin or diphtheria toxin toward lymphocytes from patients with adult T-cell leukemia. *Leukemia* 7: 553-562, 1993.
- Theuer, C.P., Kreitman, R.J., FitzGerald, D.J., and Pastan, I.: A recombinant form of *Pseudomonas* exotoxin A containing transforming growth factor alpha near its carboxyl terminus for the treatment of bladder cancer. *J. Urol.* 149: 1626-1632, 1993.
- Wang, Q.-C., Pai, L.H., Debinski, W., FitzGerald, D.J., and Pastan, I.: Polyethylene glycol-modified chimeric toxin composed of transforming growth factor alpha and *Pseudomonas* exotoxin. *Cancer Res.* 53: 4588-4594, 1993.
- Zdanovsky, A.G., Chiron, M., Pastan, I., and FitzGerald, D.J.: Mechanism of action of *Pseudomonas* exotoxin identification of a rate-limiting step. *J. Biol. Chem.* 268: 21791-21799, 1993.
- 140. FitzGerald, D. and Pastan, I.: *Pseudomonas* exotoxin and recombinant immunotoxins derived from it. *Ann. N.Y. Acad. Sci.* 685: 740-745, 1993.
- 141. Theuer, C. P., Buchner, J., FitzGerald, D., and Pastan, I.: The N-terminal region of the 37-kDa translocated fragment of *Pseudomonas* exotoxin A aborts translocation by promoting its own export after microsomal membrane insertion. *Proc. Natl. Acad. Sci. USA* 90: 7774-7778, 1993.
- FitzGerald, D. and Pastan, I.: Recombinant toxins directed to cytokine and growth factor receptors. In: Oppenheim, J.J., Rossio, J., and Gearing, A. (Eds.): *Clinical Applications of Cytokines*. Columbia, MD, Bermedica Production, Ltd., 1993, pp. 263-267.

- Kreitman, R.J., Bailon, P., Chaudhary, V.K., FitzGerald, D.J.P., and Pastan, I.: Recombinant immunotoxin containing anti-Tac(Fv) and derivatives of *Pseudomonas* exotoxin produce complete regression in nude mice of an interleukin 2 receptor-expressing human carcinoma. *Blood* 83: 426-434, 1994.
- Draoui, M., Siegall, C. B., FitzGerald, D., Pastan, I., and Moody, T.W.: TGF alpha-PE40 inhibits non-small cell lung cancer growth. *Life Sci.* 54: 445-453, 1994.
- 145. Chiron, M.F., Fryling, C.M., and FitzGerald, D.J.: Cleavage of *Pseudomonas* exotoxin and diphtheria toxin by a furin-like enzyme prepared from beef liver. *J. Biol. Chem.* 269: 18167-18176, 1994.
- FitzGerald, D.J., Fryling, C.M., Zdanovsky, A., Saelinger, C.B., Jounnas, M., Strickland, D., and Leppla, S.: Selection of *Pseudomonas* exotoxin resistant cells with altered expression of a2MR/LRP. *Ann. N.Y. Acad. Sci.* 737: 138-144, 1994.
- Battey, F.D., Gagvels, M.E., FitzGearld, D.J., Argraves, W.S., Chappell, D.A., Strauss, J.F., and Strickland, D.K.: The 39-kDa receptor-associated protein regulates ligand binding by the very low density lipoprotein receptor. *J. Biol. Chem.* 269: 23268-23273, 1994.
- Benhar, I., Wang, Q.-C., FitzGerald, D.J., and Pastan, I.: *Pseudomonas* exotoxin mutants: Replacement of surface-exposed residues in domain III with cysteine residues that can be modified with polyethylene glycol in a site-specific manner. *J. Biol. Chem.* 269: 13398-13404. 1994.
- 149. Pastan, I.H., Pai, L.H., Brinkmann, U. and FitzGerald, D.J.: Recombinant toxins: New therapeutic agents for cancer. *Ann. N.Y. Acad. Sci.* 758: 345-354, 1995.
- FitzGerald, D.J., Fryling, C.M., Zdanovsky, A., Saelinger, C.B., Kounnas, M., Winkles, J.A., Strickland, D., and Leppla, S.: *Pseudomonas* exotoxin-mediated selection yields cells with altered expression of low density lipoprotein receptor-related protein. *J. Cell Biol.* 129: 1533-1541, 1995.
- Mucci, D., Forristal, J., Strickland, D., Morris, R., FitzGerald, D., and Saelinger, C.B.: Basis for cellular susceptibility to *Pseudomonas* exotoxin A. *Infect. Immun.* 63: 2912-2918, 1995.
- Pitcher, C., Roberts, L. Fawell, S., Zdanovsky, A.G., FitzGerald, D.J., and Lord, J.M.: A potent chimeric toxin is generated by replacing domain III of *Pseudomonas* exotoxin with ricin A chain-KDEL. *Bioconjug. Chem.* 6: 624-629, 1995.
- 153. FitzGerald, D. (Ed.): Seminars in Cancer Biology, Vol. 6, 1995, 317 p.
- Gu. M., Gordon, V.M., FitzGerald, D.J.P., and Leppla, S.H.: Furin regulates both the activation of Pseudomonas exotoxin A and the quantity of the toxin receptor expressed on target cells. *Infect. Immun.* 64: 524-527, 1996
- Pastan, I., Pai, L.H., Brinkmann, U., and FitzGerald, D.: Recombinant immunotoxin. *Breast Cancer Res. Treat.* 38: 3-9, 1996.
- Zdanovsky, A. G., Zanovoskaia, M.V., Strickland, D., and FitzGerald, D.: Ligand-toxin hybrids directed to the alpha 2-macroglobulin receptor/low density lipoprotein receptor-related protein exhibit lower toxicity than native PE. J. Biol. Chem. 271: 6122-6128, 1996.
- 157. Frankel, A.E., FitzGerald, D., Siegall, C., and Press, O.W.: Advances in immunotoxin biology and therapy: A summary of the Fourth International Symposium on Immunotoxins. *Cancer Res.* 56: 926-932, 1996.
- 158. FitzGerald, D.J.: Why toxins. Sem. Cancer Biol. 7: 87-95, 1996.

- 159. FitzGerald, D. and Pastan, I.: Recombinant immunotoxins for the treatment of cancer. *J. Controlled Release* 39: 261-265, 1996.
- Mansfield, E., Pastan, I., and FitzGerald, D.J.: Characterization of RFB4-PE immunotoxins targeted to CD22 on B-cell malignancies. *Bioconjug. Chem.* 7: 557-563, 1996.
- 161. Chiron, M.F., Ogato, M. and FitzGerald, D.J.: Pseudomonas exotoxin exhibits increased sensitivity to furin when sequences at the cleavage site are mutated to resemble the arginine-rich loop of Diphtheria toxin. *Mol. Microbiol.* 22: 769-778, 1996.
- 162. Rozemuller, H., Rombouts, W.J.C., Hagenbeek, A., Touw, I.P., FitzGerald, D.J.P., Dreitman, R.J., Pastan, I., and Martens, A.C.M.: Treatment of acute myelocytic leukemia with interleukin-6 Pseudomonas exotoxin fusion protein: preclinical in vivo studies in a rat leudemia model. *Leukemia* 10: 1796-803, 1996.
- 163. Fitzgerald D.J. Antitumor immunotoxin secretion by T cells: ABSolutely FABulous? [news; comment] Comment on: *Nature Biotechnol.* 15: 46-51. *Nature Biotechnol.* 15: 18-19, 1997.
- Mansfield, E., Chiron, M.F., Amlot, P., Pastan, I., and FitzGerald, D.J.: Recombinant RFB4 single-chain immunotoxin that is cytotoxic towards CD22-positive cells. *Biochem. Soc. Trans.* 25: 709-714, 1997.
- Mansfield, E., Amlot, P., Pastan, I. and FitzGerald, D.J.: Recombinant RFB4 immunotoxins exhibit potent cytotoxic activity for CD22-bearing cells and tumors. *Blood* 90: 2020-2026, 1997.
- Terpstra, W., Rozemuller, H., Breems, D.A., Rombouts, E.J., Prins, A., FitzGerald, D.J., Kreitman, R.J., Wielenga, J.J., Ploemacher, R.E., Lowenberg, B., Hagenbeek, A., and Martens, A.C.: Diphtheria toxin fused to granulocyte-macrophage colony-stimulating factor eliminates acute myeloid leukemia cells with the potential to initiate leukemia in immunodeficient mice, but spares normal hemopoietic stem cells. *Blood* 90: 3735-3742, 1997.
- 167. Rozemuller, H., Rombouts, E.J., Touw, I.P., FitzGerald, D.J., Kreitman, R.J., Pastan, I., Hagenbeek, A., and Martens, A.C.: Sensitivity of human acute myeloid leukaemia to diphtheria toxin-GM-CSF fusion protein. *Br. J. Haematol.* 98: 952-959, 1997.
- 168. Chiron, M.F., Fryling, C.M., and FitzGerald, D.: Furin-mediated cleavage of Pseudomonas exotoxin-derived chimeric toxins. *J. Biol. Chem.* 272: 31707-31711, 1997.
- 169. FitzGerald, D.J., Fryling, C.M., McKee, M.L., Vennari, J.C., Wrin, T. Cromwell, T.E.M., Daugherty, A.L., and Mrsny, R.J.: Characterization of V3-loop Pseudomonas exotoxin human immunodeficiency virus-1. *J. Biol. Chem.* 273: 9951-9958, 1998.
- Avramoglu, R.K., Nimpf, J., McLeod, R.S., Ko, K.W., Wang, Y., FitzGerald, D., and Yao, Z.: Functional expression of the chicken low density lipoprotein receptor-related protein in a mutant chinese hamster ovary cell line restores toxicity of Pseudomonas exotoxin A and degradation of alpha2-macroglobulin. *J. Biol. Chem.* 273: 6057-6065, 1998.
- 171. Schmoelz, S., Benn, S.J., Laithwaite, J.E., Greenwood, S.J., Marshall, W.S., Munday, N.A., FitzGerald, D.J., and LaMarre, J.: Expression of hepatocyte low density lipoprotein receptor-related protein is post-transcriptionally regulated by extracellular matrix. *Lab. Invest.* 78: 1405-1413, 1998.
- 172. Ko, K.W.S., McLeod, R.S., Avramoglu, R.K., Nimpf, J., FitzGerald, D.J., Vukmirica, J., and Yao, Z.: Mutation at the processing site of chicken LDL receptor-related protein impairs efficient endoplasmic reticulum exit but proteolytic cleavage is not essential for its endocytic functions. *J. Biol. Chem.* 273: 27779-27785, 1998.

- Mrsny, R.J., Daugherty, A.L., Fryling, C.M., and FitzGerald, D.J.: Mucosal immunization with a chimera composed of Pseudomonas exotoxin and the gp120 V3 loop sequence of HIV-1 induces both salivary and serum antibody responses. *Vaccine* 17: 1425-1433,1999.
- 174. FitzGerald, D.: Recombinant immunotoxins. In Chamow, S. and Ashkenazi, A. (Eds.): *Antibody Fusion Proteins*. Wiley, 1999, pp. 111-126.
- 175. McKee, M.L. and FitzGerald, D.J.: Reduction of furin-nicked Pseudomonas exotoxin A: An unfolding story. Biochemistry 38: 16507-16513, 1999.
- Laithwaite, J.E., Benn, S.J., Yamate, J., FitzGerald, D.J., and LaMarre, J.: Enhanced macrophage resistance to Pseudomonas exotoxin A is correlated with decreased expression of the low-density lipoprotein receptor-related protein. *Infect. Immun.* 67: 5827-5833, 1999.
- Daugherty, A.L., McKee, M.L., FitzGerald, D.J., and Mrsny, R.J.: Epithelial application of Pseudomonas aeruginosa exotoxin A results in a selective targeting to cells in the liver, spleen and lymph node. *J. Controlled Release* 65: 297-302, 2000.
- 178. Kreitman, R.J., Margulies, I., Stetler-Stevenson, M., Wang, Q.C., FitzGerald, D.J., and Pastan, I.: Cytotoxic activity of disulfide-stabilized recombinant immunotoxin RFB4(dsFv)-PE38 (BL22) toward fresh malignant cells from patients with B-cell leukemias. *Clin. Cancer Res.* 6: 1476-1487, 2000.
- FitzGerald, D. and Mrsny, R.J.: New approaches to antigen delivery. Crit. Rev. Ther. Drug Carrier Sys. 17: 165-248, 2000.